THE

DYSPNŒA OF ASTHMA & BRONCHITIS:

Its Causation, and the Influence of Nitrites upon it.

BY

THOMAS R. FRASER, M.D., F.R.S., F.R.C.P.E.,

PROFESSOR OF MATERIA MEDICA AND OF CLINICAL MEDICINE IN THE UNIVERSITY OF EDINBURGH.

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DYSPNŒA OF ASTHMA AND BRONCHITIS.

Dyspnœa, or difficulty in breathing, is one of the most common of symptoms in disease, and especially in disease of the respiratory apparatus, with each of the many pathological affections of which it may be associated. My remarks, however, shall be restricted to its manifestation in asthma and bronchitis. In the former disease it presents itself as an urgent orthopnœic breathlessness, and in the latter as a sensation of constriction or weight in the chest, and a difficulty in the performance of respiration. The breathlessness, or dyspnœa, in each of these diseases is, no doubt, dependent on defective aëration of the blood, caused either by insufficient contact of air with the bloodvessels in the pulmonary vesicles, or by insufficient movement of air in the air-passages. Insufficient contact occurs, for example, when the air vesicles are filled with liquid or semiliquid contents, and it is clearly a cause that is to some extent productive of the dyspnœa of bronchitis in many of its forms and stages, as well as of the dyspnœa of several other diseases of the lungs. Insufficient movement of air occurs when the calibre of the air-passages is reduced, or when from any cause the expansion or retraction of the chest is impeded; and this imperfect movement of air is usually recognised as a cause of the dyspnœa that occurs in both asthma and bronchitis.

Asthma.

The symptoms of asthma are, indeed, typically those that are to be associated with imperfect movement of air. They have been thus described by Riegel:[1]—"The patient having gone to bed perfectly well, is suddenly awakened in the night, while sleeping quietly, by an intense sense of oppression and anxiety. Breathing is very laborious, and the respiration is attended with audible whistling and rattling, and the dyspnœa rapidly increases to an excessive degree. The cyanosis increases from minute to minute, the face becomes bluish-red and turgid, the eyeballs protrude, the patient supports himself on both arms to struggle powerfully for air, and the face becomes bathed in perspiration. The patient can no longer get his breath in the recumbent position, and often

[1] Ziemssen's *Cyclopædia of the Practice of Medicine*, 1877, vol. iv. p. 557.

assumes the most varied attitudes in order to appease in a measure his craving for air. . . . Soon the patient hurries to the window to struggle for a mouthful of fresh air. In spite of all this, he does not appease his craving for air, even by the forcible action of all his auxiliary muscles. The paroxysm continues at its height for a long time—one, two, or more hours—and then it gradually subsides. The respiration becomes easier again, the cyanosis disappears, the patient gradually feels freer and freer, and then drops off into a quiet, deep, uninterrupted sleep."

Now, what is the cause of this intense and distressing dyspnœa? No anatomical lesions are found which are sufficient to account for it. It is regarded as a functional disorder produced by alterations in normal physiological conditions, or by temporary structural changes which disappear with the asthmatic paroxysm.

Speculation has been active, however, in advancing hypotheses regarding the nature of the functional or temporary structural disturbances which so obviously produce an obstruction to the movement of air along the respiratory passages. Setting aside the theories that were originated previously to the discoveries of Lænnec and Auenbrugger in physical diagnosis, when asthma was a term applied not only to pulmonary dyspnœa, but also to the dyspnœa of diseases of the heart and large bloodvessels, of the pleura, glottis, stomach, and other organs and parts of the body remote from the lungs, it is probable that the first certain and firm basis of knowledge as to its causation was supplied by the demonstration by Reisseissen,[1] Prochaska, and Kölliker, of the existence of a muscular structure in the bronchi. The demonstration of the contractile power of this muscular structure by Williams[2] and Longet,[3] amply confirmed by the subsequent experiments of Paul Bert[4] and others, led to a revival of the old and, for a time, discredited view, that asthma is produced by a spasmodic affection of the muscles and nerves of respiration. The asthma convulsivum of Willis then became the asthma of bronchial spasm of Cullen, Romberg, Bergsen, Trousseau and Salter; and for more than half a century was the generally accepted doctrine, notwithstanding the enunciation of other theories, usually of a purely speculative character, such as those of Todd, Brée, Budd, Walshe, and others.

The most formidable attacks made on the theory of bronchial spasm, however, were probably those of Wintrich, in 1854, and of Weber, in 1872; as the important hypothesis of Leyden,[5] that the asthmatic paroxysm is produced by irritation of the vagus termina-

[1] *Ueber den Bau der Lungen.* Berlin, 1822.
[2] *Transactions of the British Association for the Advancement of Science,* 1840, p. 411.
[3] *Comptes rendus des sciences,* 1842, t. xv. p. 500.
[4] *Leçons sur la physiologie comparée de la respiration,* 1870, p. 379.
[5] Virchow's *Archiv,* 1872, Bd. 54, p. 324.

tions in the bronchi, by minute sharp-pointed crystals, involves as an explanation of the paroxysm a reflex spasm of the bronchial muscles.

Wintrich[1] denied that spasmodic contraction of the bronchi is possible, and maintained that the only explanation consistent with the phenomena is to be found in tonic spasm of the diaphragm alone, or of the diaphragm and muscles of respiration together. He was led to adopt this theory from the results of some experiments which appeared to show that the bronchi did not contract under stimulation, and from a belief that the enlargement and hyper-resonance of the lungs, which nearly all observers had recognised during the paroxysm of asthma, could not be explained by spasm of the bronchial muscles. His opinions were supported by Bamberger,[2] who further pointed out that in a few cases of asthma the lower limit of hepatic dulness remains unchanged during both expiration and inspiration, at the line of deep inspiration. Wintrich's opinions and statements have not remained unchallenged. The most damaging criticisms they have sustained have been from Biermer,[3] who justly occupies the position of being one of the ablest supporters of the old theory that asthma is caused by spasm of the bronchial muscles. Biermer has the further merit of having prominently shown that asthma is characterized by expiratory dyspnœa, which distinguishes it from the dyspnœa of obstruction in the larger air-passages, where the embarrassment is more decidedly during inspiration. He endeavours to prove that spasm of the bronchi is able to cause enlargement of the thorax, increased percussion resonance over the lungs, descent and restricted movements of the diaphragm, and relative difficulty of expiration, as contrasted with inspiration ; and thus he apparently succeeds in advancing a sufficient explanation of the phenomena of asthma.

The other most formidable opposition which the doctrine of bronchial spasm has encountered may, for convenience, be associated with the name of Weber, although his theory seems to be but a modification of that previously advanced by Traube. Weber[4] ascribed the asthmatic attack to a sudden congestive thickening of the bronchial mucous membrane through the agency of vasomotor nerves, and he compared the changes that were thereby produced to the local swelling and abnormal secretion of the nasal mucous membrane, which in many persons are produced by catarrh. In so far as the causation of the asthmatic dyspnœa is concerned, this theory also agrees with the old supposition that the retrocces-

[1] Virchow's *Handbuch der speciellen Pathologie und Therapie*, 1854, Bd. v. ; and *Krankheiten der Respirationsorgane*, Erlangen, 1855–57.

[2] *Wurzburger medicinische Zeitschrift*, 1865, Bd. vi.

[3] *Ueber Bronchialasthma, Sammlung Klinischer Vorträge*, 1875, 12, p. 39.

[4] *Ueber Asthma Nervosum. Tageblatt des* 45, *Versammlung deutscher Naturforscher und Aerzte zu Leipsic*, 1872, p. 159.

sion of certain cutaneous eruptions is productive of asthma, revived in more modern times by Waldenburg,[1] in his so-called herpetic asthma, and also by Sir Andrew Clark,[2] in a paper published last year on the theory of bronchial asthma.

The three explanations of the production of the asthmatic paroxysm, which seem at the present time to be maintained more than any others, are, therefore, embodied in the theory of bronchial spasm, in the theory of spasm of the diaphragm, associated, or not associated, with spasm of the other ordinary or extraordinary muscles of respiration, and in the theory of constriction of the bronchial tubes by swellings of a hyperæmic, herpetic, or urticaria-like character.

The existence of these contending theories is a sufficient proof of the difficulties that are encountered in explaining the dyspnœa of asthma. The observation of symptoms, the assistance that has been derived from advancements in the physiology of the respiratory and nervous systems, and the great increase in knowledge of the pharmacology of the substances that are used as remedies, do not appear to have entirely solved the difficulties. No doubt the second theory, that of Wintrich, has sustained from Biermer a more damaging criticism than either of the two others has yet met with; and it may be regarded as demonstrated that spasm of the diaphragm, combined or not combined with spasm of the muscles of respiration, is not the essential or primary cause of the symptoms of asthma, however such spasm, in some cases and in some degrees, may occur as a secondary condition during the paroxysm. That able and trained observers are divided in their belief as to the correctness of the other two theories, is shown by the statement of Dr Geddings,[3] of America, that the retrocession of cutaneous eruptions as a cause of asthma, has of late years "found but few advocates among intelligent physicians;" and of Riegel,[4] that the several grades of asthma "can be explained by the mere tumefaction of the mucous membrane, seems to me improbable;" while, on the other hand, Sir Andrew Clark[5] affirms "that the bronchial spasm theory of asthma is either inadequate to explain the phenomena of the paroxysm, or is not in harmony with the present state of physiological and pathological knowledge."

It seems obvious that some additional facts are required before the truth can be arrived at. The obtaining of such facts is desirable, not merely because of the interest that is attached to the elucidation of the pathogenesis of this as of all diseases, but much

[1] *Berliner klinische Wochenschrift*, 1873.

[2] *The International Journal of the Medical Sciences*, January 1886, vol. xci. p. 104.

[3] Pepper's *System of Medicine*, 1885, vol. iii. p. 193.

[4] Ziemssen's *Cyclopædia of the Practice of Medicine*, 1877, vol. iv. p. 554.

[5] *Loc. cit.*, p. 110.

more importantly, on account of the basis that would thereby be gained for the proper application of remedies. A very different treatment, for example, would be suggested for the cure of a dyspnœa dependent on stenosis of the bronchial tubes caused by hyperæmia, from the treatment of a dyspnœa dependent on stenosis caused by spasm of the bronchial muscles.

In considering the problem that is presented, we may assume that stenosis of the bronchial tubes is present. It is, indeed, impossible to overlook the significance of what are, after all, the most constant, as well as the most prominent, of the physical signs that accompany the asthmatic paroxysm. On auscultating the chest, there are heard râles of a snoring, cooing, and whistling character, unaccompanied during a part of the paroxysm, in most cases, by any moist sounds, and, in not a few cases, heard during the entire paroxysm unassociated with any moist sound, and even terminated, as Graves[1] has pointed out, without any expectoration whatever. The bronchi in which these sounds occur are furnished with blood-vessels which might dilate and produce hyperæmic swellings; they are also furnished with muscles which might contract spasmodically and here and there produce constrictions. The possibility of the latter causation of constriction cannot, I think, admit of a doubt, since the discoveries of the earlier investigators have been so amply confirmed by Paul Bert, and by Graham Brown and Roy.[2]

It occurred to me that in deciding between the two theories of the causation of the asthmatic paroxysm which seem at present to hold the field, some assistance might be derived by determining if the auscultatory phenomena to which I have referred can be modified, and simultaneously the dyspnœa reduced or removed by the action of any pharmacological agent that markedly influences the contractility of muscle, and especially of non-striped muscle. It is well known that many substances relieve the dyspnœa of asthma—such substances, for example, as atropine, morphine, and chloral—but their influence upon the auscultatory phenomena has not, so far as I know, been investigated. In the case of the substances I have mentioned investigation of this kind is not, indeed, likely to afford distinct or incisive results, as their influence on the dyspnœa is uncertain, and usually, but slowly, produced, and as they involve in their sphere of action many parts of the nervous system; while it has not been proved that independently of this involvement they influence the contractility of non-striped muscle in a very distinct or powerful manner.

In the absence of evidence of the existence of any substance that rapidly and distinctly modifies the contractility of the bronchial tubes, the analogy in structure and nerve relationship between the bloodvessels and the bronchial tubes, suggested that the most appropriate substances to be employed for the purpose I have

[1] *Clinical Lectures on the Practice of Medicine*, 1864, p. 507.

[2] *The Journal of Physiology*, vol. vi., 1883; Appendix, p. xxi.

stated would be those which are capable of modifying the contractility of bloodvessels by direct contact with them. Nitrite of amyl has been shown to possess this action, and the probabilities are in favour of its being possessed also by other nitrites and by substances that have essentially the same pharmacological action.

It seemed advisable to ascertain positively, in the first place, if all the chief nitrites possess this action, and if so, to what extent they severally exert it. I was fortunate in inducing Mr Sillar to undertake a series of experiments having these objects in view. The experiments entailed a large amount of patient observation, and they were made with great care and with every precaution to insure accuracy. The mode of procedure was as follows:—The brain and spinal cord having been destroyed in a frog, the heart of the animal was exposed and all the bloodvessels connected with it, except the left aorta, and the veins opening into the sinus venosus were ligatured. A canula was then tied into the left aorta and connected with a tube leading to reservoirs, placed always at the same height above the frog. The contents of any one of the reservoirs could be caused to flow into the aorta by opening or shutting clamps that were placed on the tubes leading from the reservoirs. The rate of flow of a saline solution through the entire vascular system of the animal was first ascertained, and then a solution of the same saline containing a given quantity of a nitrite was substituted for the simple saline solution, and its rate of flow through the bloodvessels of the animal was ascertained. By this procedure the effects of contact of any strength of a solution of nitrite upon the bloodvessels could be exactly determined; for if the rate of flow were diminished, it would be shown that the bloodvessels had been caused to contract, whereas, if the rate of flow were increased, it would be shown that the bloodvessels had been caused to dilate. The nitrites that were tested were nitrite of amyl, nitrite of ethyl, and nitrite of sodium. Without entering into details, I will content myself with stating that the general result was that each of these nitrites produced by contact a decided dilatation of the bloodvessels, in a few instances so great that the passage through them of the solution was doubled in its rate; and that dilatation occurred, usually in less than a minute after the nitrite had entered the bloodvessels, and was continued for periods varying from thirty to ninety minutes. Nitrite of sodium was found to be the least powerful, and nitrite of amyl the most powerful dilator of bloodvessels, nitrite of ethyl occupying an intermediate position. The difference is indicated by the statement that whereas a solution of 1 in 100,000 of nitrite of amyl was sufficient to cause a marked increase in the rate of flow through the bloodvessels—indicating a distinct dilatation of their walls—it was necessary to employ a solution of 1 in 10,000 of nitrite of sodium to produce a nearly equal effect.

The action of nitro-glycerine was not examined in the same manner, as the conditions probably required to effect its conversion into a nitrite, which exist in the blood of a warm-blood animal, could not be obtained in the saline solutions substituted for the blood in these experiments.[1]

A few experiments were, however, also made with alcohol and chloroform. Somewhat concentrated solutions of the former produced dilatation; but no constant results were obtained with chloroform, the evidence, on the whole, pointing to an absence of any dilatation under the contact of this substance with the blood-vessels.

It was thus shown that very dilute solutions of nitrites, apart altogether from any influence they may exert on structures at a distance, produce dilatation of the walls of bloodvessels as a result of contact with them. If they could be shown likewise to modify in asthma the condition of the bronchial tubes, whose anatomical relations to bloodvessels are so marked, it is obvious that an important step would be gained in deciding which of the theories of the causation of the asthmatic paroxysm is the correct one. In the absence of any direct experimental method for ascertaining the state of the bronchi, and especially for estimating the changes that might be produced in them by medicinal agents, during an asthmatic paroxysm, it seemed to me that the observation of the auscultatory phenomena, which have, by nearly universal consent, been explained by stenosis of the bronchi, would be likely to supply important evidence.

My first observation was made in 1880, on a patient, Jessie L., twenty-two years of age, suffering from asthma and from excitement of the circulation and slight enlargement of the thyroid gland. She was one of three sisters who presented, in various forms, the symptoms of exophthalmic goitre. The dyspnœa had lasted for several weeks; it was most severe at night, but occasionally manifested itself during the day. When the observation was made (August 14, 1880) she was sitting up in bed suffering from great breathlessness. The pulse was 100 and the respirations 28 per minute. On auscultating the front of the chest, it was found that expiration was markedly prolonged, and that both inspiration and expiration were accompanied with cooing, whistling, and creaking râles, and with occasional medium crepitations.

At 1 55′ P.M. she began to inhale 10 minims of nitrite of amyl placed on blotting-paper at the bottom of a small glass tumbler, and she continued inhaling for about one minute and fifty seconds,

[1] Since this sentence was written, Dr Atkinson, in the course of an elaborate research on nitrites made in my laboratory, has found, in experiments similar to those above described, that nitro-glycerine in very dilute solutions powerfully dilates the arteries and capillaries. This local action of nitrites has also been recently shown to occur in warm-blooded animals by R. Kobert (Ueber die Beeinflussung der peripheren Gefässe durch pharmakologische Agentien. *Archiv für experimentale Pathologie und Pharmakologie*, Bd. 22, 1886, p. 77).

the chest being continuously auscultated during the observations.

At 1 56′ 30″, the face was flushed, and the pulse was 120 per minute.

At 1 57′, the cooing, whistling, and creaking râles had entirely disappeared, and the patient spontaneously remarked that her breathing was easier, and that the sensation of tightness had disappeared from the chest.

At 1 58′, the râles had returned, but as yet to only a slight extent; the breathing had become more difficult, and the pulse was 95 per minute.

At 2 4′, the pulse was 96, and the respirations 28 per minute, while the breathing was as difficult, and the râles as loud and continuous as they had been before the inhalations.

From 2 6′ to 2 7′ she again inhaled nitrite of amyl.

At 2 6′ 30″, the face was flushed.

At 2 6′ 45″, the flushing had increased, the râles in the chest had entirely disappeared, and the patient stated that the breathing was perfectly easy.

At 2 6′ 50″, the pulse was 122, and the respirations 30 per minute, while the breath sounds were still unaccompanied with râles.

At 2 9′, cooing sounds were occasionally heard.

At 2 11′, the cooing sounds continued, but the breathing was still easy.

At 2 12′, the breathing was embarrassed, and cooing, creaking, whistling, and crepitant râles were audible, though they were not so continuous as immediately before the second inhalation.

At 2 19′, the pulse was 95, and the respirations 30, while the auscultatory phenomena and the difficulty of breathing were as pronounced as before the administration of nitrite of amyl.

From 2 22′ to 2 23′ she, a third time, inhaled nitrite of amyl.

At 2 22′ 30″, the face was very red.

At 2 22′ 50″, the pulse was 126, and the respirations 23 per minute, while the râles had entirely disappeared, and the breathing was again, in her own words, "quite easy."

At 2 25′, the pulse was 90, and the respirations were 28 per minute; the redness of the face had completely disappeared, the breathing was slightly embarrassed, and cooing and creaking râles were occasionally heard.

At 2 28′, the breathing was as much embarrassed as it originally had been; and with the return of dyspnœa there was a complete return of the auscultatory phenomena that had been present before the first inhalation of nitrite of amyl.

There had been no cough nor expectoration from the commencement to the termination of the observations. The patient stated that the breathlessness and sense of tightness in the chest had been entirely removed for a time by the inhalations, and the only unpleasant effect they seem to have produced was a briefly lasting sense of fulness in the head.

To illustrate more clearly the relationship between the effects on the asthma and on the circulation, I would refer to the pulse-tracings taken frequently during the observations (Figs. 1 to 12). They show, in a very remarkable manner, a coincidence between the fall of blood tension and the cessation of the dyspnœa and auscultatory phenomena, and also between the return to the original state of the blood tension and the reappearance of the dyspnœa and auscultatory phenomena. As the lowered blood tension is accompanied with acceleration of the heart's contractions, it can only be accounted for by the dilatation of bloodvessels.

FIG. 1.—Before first inhalation. Pulse 100, respirations 28 per minute. Breathing much embarrassed, râles abundant.

NITRITE OF AMYL INHALED DURING NEARLY TWO MINUTES.

FIG. 2.—Two minutes after inhalation commenced. Pulse 120 per minute. Breathing quite easy. No râles.

FIG. 3.—One minute after inhalation ceased. Pulse 96 per minute. Breathing slightly embarrassed. Râles occasionally heard.

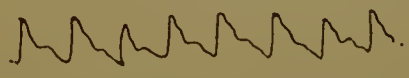

FIG. 4.—Seven minutes after inhalation ceased. Pulse 96, respirations 28 per minute. Breathing embarrassed. Râles nearly continuous.

SECOND INHALATION OF NITRITE OF AMYL DURING TWO MINUTES, BEGUN NINE MINUTES AFTER THE FIRST INHALATION CEASED.

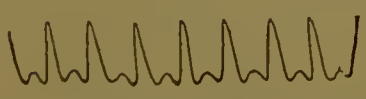

FIG. 5.—Fifty seconds after second inhalation commenced. Pulse 122, respirations 30 per minute. Breathing perfectly easy. No râles.

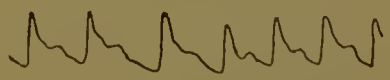

FIG. 6.—Two minutes thirty seconds after second inhalation ceased. Pulse 96, respirations 28 per minute. Breathing easy. Occasional râles.

FIG. 7.—Eight minutes after second inhalation ceased. Pulse 96, respirations 30 per minute. Breathing embarrassed. Râles more frequent.

FIG. 8.—Twelve minutes after second inhalation ceased. Pulse 95, respirations 30 per minute. Breathing embarrassed. Râles abundant.

Third Inhalation of Nitrite of Amyl during One Minute, begun Fifteen Minutes Thirty Seconds after Second Inhalation ceased.

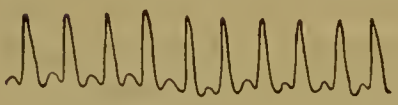

Fig. 9.—Fifty seconds after third inhalation commenced. Pulse 126, respirations 23 per minute. Breathing quite easy. No râles.

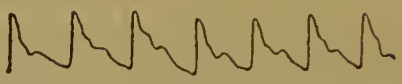

Fig. 10.—Two minutes after third inhalation ceased. Pulse 90, respirations 28 per minute. Breathing easy. Râles only rarely.

Fig. 11.—Five minutes after third inhalation ceased. Pulse 90, respirations 28 per minute. Breathing embarrassed. Râles abundant.

Fig. 12.—Eighteen minutes after third inhalation ceased. Pulse 88, respirations 28 per minute. Râles very abundant.

Several observations were made on other patients suffering from asthmatic dyspnœa, by administering nitrite of amyl or nitrite of ethyl by inhalation. The results generally corresponded very closely with those described in the above observation.

It is apparent that, although the effects are of the greatest significance in regard to one of the main objects for which the observations had been made, they were, at the same time, of a very transient duration. Before any further observations had been made on asthma, I had, however, succeeded in collecting a number of facts which rendered it probable that effects of a more lasting description, and therefore of greater value to therapeutics, might be obtained were the nitrites administered through the mouth or stomach. The observations in which this method of administration was followed derive an additional importance from the circumstance that they were made on patients during extremely severe dyspnœa, of a markedly orthopnœic character. These severe attacks occurred only during the night or the early hours of the morning. The occasions of their occurrence were somewhat irregular, so that it could not be anticipated with certainty that they would occur on any special night. It was, therefore, necessary to entrust the observations to those who could, at any moment, make them. They were kindly undertaken by Dr Vaughan, who was at the time acting as my resident physician at the Royal Infirmary, and by Mr Tofft, a clinical clerk in my wards, who remained in the hospital during several nights for the purpose. Both gentlemen had previously assisted me in many observations of this kind, and they were, therefore, thoroughly qualified to undertake the work.

An interesting and complete series of observations was made on a man, Hugh G., forty years of age, who had suffered from asthma for four years, and had been an inmate of the Royal Infirmary for three months. As one generally finds in cases of so long duration,

emphysematous changes had been produced in the lungs, and symptoms of bronchitis were also present. The emphysema was, however, only moderate and the bronchitis slight, and frequently, for days, the symptoms of the latter were entirely absent. His sputum was usually tenacious and gelatinous, and small in quantity. Several times in each week his sleep was interrupted by severe attacks of breathlessness, which lasted from an hour and a half to three hours, and sometimes occurred twice or even thrice in one night. During the attacks the patient either sits up in bed or walks about the ward, sitting down at times to recover strength. He struggles violently for breath, inspiration and expiration succeed each other rapidly for a short time, then expiration becomes brief, the chest seems to become rigid in full inspiration, violent respiratory efforts are made with but little change in the volume of the thorax, and the extraordinary muscles of respiration are brought into play with but little result. After this state has lasted for some time, endeavours are made to cough, which are at first unsuccessful, but after a number of gasping and strained inspirations and expirations, he at last succeeds in coughing, and soon a small quantity of frothy and tenacious sputum is expectorated, when the patient either at once or soon after obtains relief. During the greater part of the paroxysm, the face and neck, and to a less extent the chest, are much congested.

Observation II.—On the 30th of December, 1886, a paroxysm began at about 4 30′ A.M. When the patient was examined, eight minutes afterwards, he was sitting up in bed holding his sides, and so breathless that he could scarcely speak. The veins of the neck were turgid, and the laboured breathing was accompanied with loud wheezing audible in the corridor of the ward at a distance of at least forty yards from the patient. The pulse was 120 per minute and feeble, and the respirations were 36 per minute.

At 4 41′, both sides of the chest were auscultated, with the result that the ordinary breath sounds were everywhere supplanted, during both inspiration and expiration, by continuous rhonchi and sibili. The time-relation of inspiration to expiration was $1 : 1\frac{1}{2}$.

At 4 43′, five minims of nitrite of amyl in two drachms of water were given to the patient.

At 4 43′ 30″, at the left side of the chest, the rhonchi and sibili had markedly diminished; at the right side there were no accompaniments whatever, with the exception of a few medium crepitations at the end of expiration. The face, hands, and chest were distinctly flushed.

At 4 44′, the pulse was 96, and fuller, and the respirations were 24 per minute. The patient said that his breathing was greatly relieved.

At 4 45′ 30″, the breathing at the right side was absolutely

clear and vesicular; and at the left side there was only a slight sibilus during inspiration, expirations being free from accompaniments. The wheezing had by this time practically disappeared.

At 4 50′, the time-relation of inspiration to expiration was $1\frac{1}{2}$ to $2\frac{1}{2}$.

At 4 51′, there were no accompaniments whatever at any part of the chest either during inspiration or expiration, except a few medium crepitations that occurred at varying intervals and at both sides.

At 4 53′, at the right side, the breath sounds continued clear, except that now and then a distant rhonchus was heard at the beginning of expiration; at the left side, however, there was sibili throughout expiration and rhonchi during a part of inspiration.

At 4 55′, the patient stated that his breathing had become a little more difficult than it had been a short time before, and he referred the difficulty to the upper half of the sternum.

At 4 58′, the pulse was 90 and the respirations were 22 per minute, and the former was irregular in the character of the pulsations.

At 5 A.M., at the right side, there were no accompaniments excepting medium crepitations; and at the left side there was only a brief sibilus, sometimes with inspiration and at other times with expiration.

At 5 8′, the patient said he felt perfectly well.

At 5 14′, at the right side, there was a short rhonchus at the beginning of expiration, but no accompaniment whatever at the left side. The patient was now lying on the back no longer propped up. He seemed quite free from any difficulty in breathing, and he was apparently desirous to be allowed to sleep.

He was again seen at 6 10′, when he seemed to be, and expressed himself as being free from dyspnœa, but on auscultating the chest a few sibili and rhonchi were occasionally heard.

On the following day the patient was very well. His breathing was unembarrassed, but he experienced a little palpitation, and he said he had found it necessary to empty his bladder more frequently than he usually did.

Observation III.—On the same patient the following observations were made with nitrite of ethyl (nitrous ether).

On the 8th of January 1887, difficulty of breathing began to be experienced soon after 2 A.M.

At 3 15′ A.M., the patient was propped up in bed, breathing with great difficulty and showing signs of much distress. This difficulty was felt both in the act of inspiration and of expiration, but it was rather more in that of expiration, or, as the patient described it, "it was worse to get the breath out." There was also loud wheezing. A small quantity of sputum had been expectorated, which was tenacious and of a yellowish colour.

At 3 20′, on auscultation, rhonchi and sibili were heard during inspiration and expiration over both sides of the chest, but rather louder over the right than the left side. The pulse was 96 and the respirations were 22 per minute. The relation of inspiration to expiration was $\frac{3}{4} : 1\frac{1}{2}$ on both sides.

At 3 26′, ten minims of a 25 per cent. alcoholic solution of nitrite of ethyl, mixed with two drachms of water, were taken by the patient.

At 3 26′ 30″, patient said he was "not so ill."

At 3 28′, at both the right and the left sides, there were rhonchi with expiration, sibili had disappeared, and no accompaniments were heard with inspiration. The time-relation of inspiration to expiration was even on the right side, 1 : 1; and on the left, $\frac{3}{4} : 1$.

At 3 31′, the pulse was 89 and the respirations were 24 per minute.

At 3 35′, at both sides, a short rhonchus was heard with inspiration, but nothing with expiration. There was also only slight wheezing, and the patient exclaimed, "I'm almost quite easy now."

At 3 36′ 30″, both sides of the chest were entirely free from accompaniments. The time-relation of inspiration to expiration was at the right side, $1\frac{1}{4} : 1$; and at the left side, $1 : \frac{3}{4}$.

At 3 41′, the pulse was 72, the respirations were 24 per minute, and the breathing was still quite clear and free from accompaniments.

At 3 51′, the patient remarked that he was "quite easy," and had "no difficulty in the least" with his breathing; on auscultation, no accompaniments were anywhere to be heard; there was no wheezing; and the time-relation of inspiration to expiration was $1 : \frac{3}{4}$. The chest was frequently auscultated from this time until 4.50 A.M., and the breathing was always found to be soft and vesicular in character, and to be entirely free from rhonchi or sibili, while during the whole of this time the patient remained entirely free from dyspnœa.

At 4 52′, slight wheezing reappeared, the pulse was 72 and the respirations were 20 per minute; and the time-relation of inspiration to expiration was, at the right side, $1 : 1\frac{1}{2}$; and at the left side, $\frac{3}{4} : 1$.

At 4 55′, at the left side, slight sibilus was occasionally heard on inspiration, but there were no accompaniments at the right side.

At 5 A.M., the auscultatory phenomena were the same as at last note, but the wheezing was more audible, and expiration seemed slightly more prolonged. The patient coughed at this time, without expectorating, however.

At 5 11″, at the right side, there was slight sibilus at the beginning of inspiration with loud rhonchus during expiration, and at the left side, while inspiration was clear there were rhonchi with expiration. The breathing was now a little embarrassed.

At 5 18′, there were a few slight rhonchi and sibili, varying

much in the time of their occurrence, at both sides of the chest. The patient at one time said the breathing "is quite easy," and at another that it was "a little difficult." The pulse was 78 and the respirations were 24 per minute. He was, however, lying in a normal position in bed.

These conditions remained unchanged until 5 25′, when the observations were stopped.

Observation IV.—An observation with nitrite of ethyl was again made on this patient, on the 24th of January 1887. On this occasion, the first symptoms of an asthmatic paroxysm began to show themselves soon after midnight.

At 12 35′ A.M. the patient was sitting up in bed, supporting himself on both elbows, and breathing with great difficulty. He stated that this difficulty was more pronounced during expiration than inspiration. There was loud wheezing, audible in the corridor of the ward, at least thirty yards from the patient's bed. A little sputum had been expectorated, consisting of dark masses of a gelatinous substance.

At 12 40′, on auscultation, it was found that at the right side there were numerous rhonchi and sibili with both inspiration and expiration; and that at the left side, sibili were almost continuous through inspiration and expiration. The time-relation of inspiration to expiration at both sides was $\frac{3}{4} : 1\frac{1}{4}$. The pulse was 79, and the respirations were 30 per minute.

At 12 50′, the patient received 10 minims of a 25 per cent. alcoholic solution of nitrite of ethyl in a little water.

At 12 51′, he said, "The breathing is easier." At both sides rhonchi were heard during both inspiration and expiration, but there were no sibili. The time-relation of inspiration to expiration was at the right side, $\frac{3}{4} : \frac{3}{4}$; and at the left side, $\frac{1}{2} : \frac{3}{4}$.

At 12 54′, the wheezing had become slight. The pulse was 75 and the respirations were 24.

At 12 57′, the breath sounds were at both sides quite clear, almost vesicular in character, and entirely free from accompaniments. The time-relation of inspiration to expiration was at the right side, $1 : \frac{3}{4}$; and at the left side, $\frac{3}{4} : \frac{3}{4}$.

At 1 A.M. there was no wheezing, and the breath sounds were everywhere vesicular in character. The patient was able to lie down in a normal posture. The pulse was 72, and the respirations were 20 per minute.

At 1 6′, at the right side, an occasional slight and distant rhonchus was heard at the end of the expiration; and on the left side a similar sound at the commencement of inspiration. Slight wheezing was also audible.

At 1 11′, the conditions were the same as at 1 6′.

At 1 14′, patient said he felt "quite free" in his breathing. The pulse was 72, and the respirations were 20 per minute.

At 1 18′, the patient said the breathing was "soft as if it was oiled." There were no accompaniments on auscultation; the wheezing had quite disappeared; and the time-relation of inspiration to expiration was, on both sides, $1\frac{1}{2} : 1\frac{1}{2}$.

The patient was not again examined until 2 A.M. In the interval he had remained perfectly well, and free from any difficulty of respiration. On auscultation, the breathing was everywhere vesicular in character and without any accompaniment. The pulse was 64, and the respirations were 21 per minute. On the same day at 1 P.M., the breath sounds were also perfectly normal; there was no dyspnœa, and the time-relation of inspiration to expiration was $2 : 1\frac{1}{2}$.

OBSERVATION V.—This patient when suffering, on another occasion, from a severe paroxysm of asthma, was treated with nitrite of sodium. The paroxysm began to manifest itself at about a quarter to two in the morning of the 30th of December 1886.

At 2 54′ A.M., he was sitting up in bed in great distress, suffering from a sense of great straining in the epigastrium, and he was wheezing as loudly as before the other observations that have been described. Sputum of a very tenacious character and somewhat blood-stained was being expectorated with great difficulty. The pulse was feeble, intermittent, and extremely varying in volume. Its rate was 84, and that of the respirations 30 per minute. The time-relation of inspiration to expiration was $1 : 2\frac{1}{4}$.

At 3 A.M., there was heard on auscultation at the right side, rhonchi throughout inspiration and expiration; and at the left side, coarse rhonchi with inspiration, and rhonchi and sibili with expiration. Sibili were apparently also being produced in the throat.

At 3 2′, ten minims of a 10 per cent. solution of nitrite of sodium, mixed with a drachm of water, were given to the patient.

At 3 3′, the right side was almost free from accompaniments, but at the left side there was heard a faint rhonchus at the end of inspiration, and an occasional faint sibilus at the end of expiration. Patient "feels a lot easier."

At 3 4′, wheezing was no longer audible, and the patient said he was "quite easy." The pulse was 84 per minute, still intermittent, but a little fuller. The respirations were 30 per minute.

At 3 6′, the time-relation of inspiration to expiration at the right side was $1 : \frac{3}{4}$; and at the left side, 1 : 1.

At 3 7′, the patient said "I feel nothing at all." The breathing was quite soft and subdued at both sides, and there were no accompaniments at all.

At 3 8′, there was slight wheezing in the throat, but the breath sounds over the lungs were perfectly normal and vesicular.

At 3 12′, the patient was talking quite comfortably, and he stated that he had "no distress whatever."

At 3 13′, a small quantity of tenacious sputum was expectorated which "came quite easy."

At 3 15′, the breath sounds were still quite free from accompaniments, except that a few crepitations were heard at the beginning of inspiration over the right lung. The time-relation of inspiration to expiration was at the right side, 1 : ¾; and at the left side, 1 : ½.

At 3 17′, the pulse was 72 per minute, and rather more intermittent than formerly, and the respirations were 26 per minute.

At 3 20′, the patient continues to "feel nothing at all."

At 3 28′, the breathing was soft on both sides without any accompaniment. The time-relation of inspiration to expiration was at both sides, 1 : 1. The pulse was 79, and the respirations were 25 per minute.

At 3 51′, the conditions were the same as at last note.

At 3 53′, the breathing was still absolutely clear and soft. The time-relation of inspiration to expiration was at the right side, 1½ : ½; and at the left side, 1½ : ½.

At 4 7′, the condition of respiration was the same.

At 4 26′, the breath sounds were perfectly soft and normal. The pulse was 72, and the respirations were 21 per minute. The time-relationship of inspiration to expiration was at the right side, 1½ : 1; and at the left side, 1 : ¾.

The observations were now interrupted until 5 53′ A.M., when it was found that slight wheezing was again audible, and that over both lungs occasional and slight rhonchi and sibili were present. The patient stated that about five minutes previously he felt tightness of the chest and wheezing "come on all at once."

At 5 56′, there were faint sibili with both inspiration and expiration at the right side, and with inspiration alone at left side. The pulse was 78, and the respirations were 20 per minute. The time-relationship of inspiration to expiration was at the right side, 1 : 2; and at the left side, 1 : 1¼.

At 6 5′, the patient said "the breathing is getting tighter," and the breath is "worse to come up than go down." Over both lungs sibili were heard throughout inspiration, and the time-relation of inspiration to expiration was at both sides, 1 : 1¼.

As the asthmatic condition was obviously returning, after an absence of at least two hours and a half, it appeared of interest to determine if the return could be checked and a normal state again produced by a second administration of nitrite. The dyspnœa being as yet but slight, it seemed sufficient to administer only half the original dose of nitrite of sodium.

At 6 8′, therefore, five minims of the same 10 per cent. solution, or half a grain of nitrite of sodium, were given to the patient in a drachm of water.

In less than a minute he exclaimed, "Its away."

At 6 9′, it was found, on auscultating, that all accompaniments

had vanished from both sides, the breathing having become perfectly soft. The time-relation of inspiration to expiration had also become altered, for at the right side it was 1 : 1; and at the left side, 1 : ¾, showing a diminution in the duration of expiration.

The patient was finally seen at 7 15′ A.M. He had continued quite well since he had received the second dose. There had been no wheezing, nor sense of tightness, nor any form of difficulty in respiration. On auscultating over both lungs, it was found that the breath sounds were perfectly clear and soft, although a few small crepitations occurred early in expiration at the right side. The pulse was 78, and the respirations were 24 per minute. The time-relation of inspiration to expiration was at both sides, 1 : 1½.

OBSERVATION VI.—While this patient was suffering from a severe attack of orthopnœa, an observation was made on him with nitro-glycerine. The attack began at 2 A.M., on a damp and cold night (December 28, 1886). When he was seen at 2 35′ A.M. he was sitting upright in bed, holding on to it, and breathing with extreme difficulty, the difficulty being, as he described it, during both inspiration and expiration. There was also a cough which, after great and prolonged efforts, brought up sputa, copious in amount, muco-purulent, stained with blood, and very tenacious. It was found, on auscultation, that loud and continuous sibili occurred in both lungs during inspiration and expiration.

At 2 41′, he received two and a half minims of a one per cent. solution of nitro-glycerine diluted with a drachm and a half of water.

Almost immediately thereafter he exclaimed, "Oh! it's easier," and the wheezing had almost disappeared in a few seconds subsequently.

At 2 42′, inspiration and expiration were in both lungs very much softer, sibili had almost disappeared, slight subdued rhonchus was heard at the beginning of expiration, and there were some crepitations. The pulse was 96, and the respirations were 36 per minute.

At 2 45′, at the right side, there was slight rhonchus throughout inspiration, and at the left side short rhonchus at the beginning of inspiration. The pulse was 78, and the respirations 24 per minute.

At 2 47′, wheezing had again become audible, an attack of difficult coughing occurred, and the patient stated that the breathing was again tight, but in a few seconds afterwards he said that the tightness had disappeared. The pulse was 77, and the respirations 24 per minute.

At 2 54′, the breath sounds were absolutely clear, soft, and vesicular, and without any accompaniment.

At 3 2′, while the breath sounds at the right side were perfectly

normal, at the left side there were slight distinct rhonchi at the beginning of inspiration and expiration. The patient experienced a little tightness of breathing, but only during a few seconds.

At 3 6′, at both sides, there were distant sibili throughout inspiration and expiration.

At 3 10′, another attack of violent coughing occurred, when a little sputum was expectorated. The pulse was 86, and the respirations 24 per minute.

At 3 12′, there was again marked wheezing, and rhonchi were heard during inspiration and expiration over both lungs.

The observations were continued until 5 35′, and they showed a gradually increasing development of breathlessness and of the respiratory accompaniments, but neither attained the severity and urgency which had characterized them before nitro-glycerine had been administered.

Observation VII.—The effects of nitro-glycerine were well illustrated in another patient, Thomas H., thirty-six years of age, a well-built, muscular man, a joiner by occupation, whose illness had begun about fourteen weeks before the observation was made. There was no history of hereditary predisposition to asthma, and no personal history of pulmonary disease, with the exception of a single attack of acute pneumonia which had occurred four years previously. The patient referred the origin of the asthma to a "severe cold," following exposure to a heavy rain. A week afterwards the dyspnœa appeared, and paroxysms of asthma occurred regularly every morning at 6 o'clock, and lasted for about three hours. He also had considerable dyspnœa during the greater part of nearly every day, and especially when the weather was foggy, which prevented him from working or going about, but produced no discomfort while he was at rest beyond a sense of tightness and weight in the chest. He was free from cough and had no sputum, excepting when the dyspnœa was present, and at these times his sputum was pretty copious, watery, and frothy. No evidence was obtained of enlargement of the heart; but, although the chest was well formed, the lungs were slightly emphysematous. Expansion was good, expiration was a little prolonged, and, generally, rhonchi and sibili with medium and small crepitations were audible over the greater part of the chest. The patient also suffered from headaches, which occurred in the morning after the commencement of each paroxysm, and usually disappeared toward the afternoon.

The case was, therefore, one in which chronic bronchitis was also present, and on several occasions, after the patient's admission into the hospital, observations were made while there were no paroxysms of asthma on the influence of nitrites on the symptoms of bronchitis, to some of which I shall afterwards refer. The influence of nitrites and the conditions in which the patient was placed in the hospital, appeared to lessen the severity of the

asthmatic paroxysms ; they became less frequent, the time of their occurrence lost the regularity it had originally possessed, the bronchitis disappeared, and the patient was dismissed on December 26, 1886, apparently cured of both asthma and bronchitis, as he had no symptoms of either disease for ten days.

After returning to his home in Edinburgh, he remained well until the 28th of December. On that day, although he had not resumed work or undergone any exposure, severe dyspnœa appeared at 3 o'clock in the afternoon, and continued until 9 o'clock on the following morning. He, therefore, again came to the hospital, and was readmitted. He remained free from dyspnœa during the afternoon, but towards evening the breathing gradually became difficult, until at about 11 30′ P.M. the difficulty had increased to orthopnœa, and the patient was obliged to sit upright in bed, supporting himself with his extended arms.

At 1 12′ A.M., the patient was in great distress, feeling, as he said, "like to choke." He stated that the difficulty in breathing was felt chiefly during expiration. He had spat a small quantity of slightly adhesive sputum. There was loud wheezing, and when the chest was auscultated sibili were heard throughout inspiration and expiration at both sides, completely masking all other sounds. The pulse was 112, and the respirations 30 per minute. The time-relation of inspiration to expiration was 1 : 3.

At 1 20′, he received five minims of a one per cent. solution of nitro-glycerine mixed with two drachms of water. There was a perfect "storm" of accompaniments when the nitro-glycerine was given. In less than thirty seconds he said, "I feel a little easier."

At 1 21′ 30″, the wheezing was less audible, and at the left side inspiration was almost clear, but there were rhonchi with expiration.

At 1 23′, the breathing was almost clear at the right side, and there was a brief sibilus on expiration at the left side. Patient said he "feels much easier."

At 1 23′ 30″, at the right side there were sibili during expiration; and at the left side, sibili during inspiration. The pulse was 114, and the respirations were 30 per minute.

At 1 26′, headache came on.

At 1 27′, he expectorated about half an ounce of frothy and slightly tenacious sputum.

At 1 28′, at the right side both inspiration and expiration were vesicular and free from accompaniments; and at the left side inspiration was perfectly clear, but very slight rhonchus occurred with expiration. The wheezing was scarcely audible, and the patient said he was "a great deal easier."

At 1 31′, the pulse was 108 and the respirations were 30 per minute. The patient said the difficulty of expiration was "nothing to speak of."

At 1 34′, the breathing was at times perfectly free from accompaniments, and then for a few seconds sibili or rhonchi were heard on one or other side of the chest. The pulse was 108 and the respirations were 28 per minute. The time-relation of inspiration to expiration was 1 : 2½.

At 1 38′, the chest was beginning to feel tight, and the wheezing was distinctly audible.

At 1 42′, the breathing had become "a great deal stiffer"; the difficulty, according to the patient, was in "getting out breath." Over both lungs rhonchi and sibili were heard during inspiration and expiration.

At 1 50′, the above sounds were only occasionally heard, and the patient said he "feels as free as ever he was;" and his appearance was again that of ease.

At 2 2′, 2 14′, 2 27′, and 2 44′, the auscultatory phenomena continued as at last note. At 2 14′, the pulse was 106 and the respirations were 24 per minute; and at 2 27′, they were 80 and 25 per minute respectively.

At 2 58′, the time-relation of inspiration to expiration was, at the right side, 1 : 1; and at the left side, 1½ : 2½. The character of the breathing was soft, but now and again a brief sibilus was heard, with small crepitations at the end of expiration.

At 3 15′ and 3 57′, the conditions remained as at the last note. At the latter time the pulse was 80 and the respirations were 29 per minute; and the time-relation of inspiration to expiration was, at left side, 1 : 2.

The patient was now left to himself, apparently free from any obvious sign of dyspnœa, but still, on being asked, confessing to a sensation of slight constriction in the chest.

When he was again seen, at 4 30′ and 5 20′ A.M., he was sound asleep and breathing quietly and without wheezing.

Observation VIII.—The last case I shall describe is one which illustrates the close relationship frequently observed between bronchitis and asthma. The patient was a man, Robert B., fifty-two years of age, presenting the ordinary symptoms of pronounced emphysema and severe bronchitis, and suffering greatly from frequent periodic attacks of dyspnœa and orthopnœa. The bronchitis was manifested by coarse and medium crepitations, continuous rhonchi and sibilations, and severe cough, accompanied with an abundant mucopurulent and frothy sputum. The asthma manifested itself in paroxysms of urgent orthopnœa, occurring during the night and almost every night, and so prolonged that the patient could not obtain sleep, except in the morning and during the day.

On the 8th of January, 1885, one of the usual paroxysms began at 9 P.M. He was seen immediately afterwards, when he was sitting up in bed in great distress, with loud wheezing respiration; and it was found that rhonchi and sibili were abundantly present.

At 9 30′ P.M., a pulse tracing was taken—the pulse being 64 and the respirations 21 per minute. (Fig. 13.)

Fig. 13.—Robert B. Before nitrite of sodium. Pulse 64, respirations 21 per minute.

At 9 35′, five grains of nitrite of sodium dissolved in one drachm of water were administered.

Almost immediately afterwards, the patient felt some peculiar sensations, which he described as "the medicine going all over him and making him feel queer." In the course of a few minutes the dyspnœa was relieved, the rhonchi and sibili had entirely disappeared, and the respiratory movements were more full and more easily performed. The patient soon lay down on the bed and seemed disposed to sleep.

The pulse showed the following characters at thirty minutes, at one hour, and at one hour and a half after the nitrite had been administered. (Figs. 14, 15, and 16.)

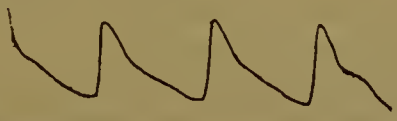

Fig. 14.—Robert B. Thirty minutes after nitrite of sodium. Pulse 76, respirations 20 per minute.

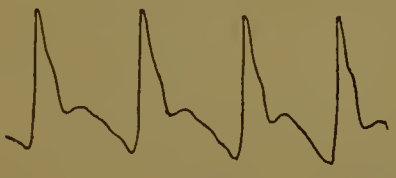

Fig. 15.—Robert B. One hour after nitrite of sodium. Pulse 76, respirations 18 per minute.

Fig. 16.—Robert B. One hour and a half after nitrite of sodium. Pulse 72, respirations 17 per minute.

The chest was frequently auscultated, and it was found to remain free from rhonchi and sibili during two hours succeeding the administration. After this time rhonchi were again heard, but only in a subdued form. The patient, however, was so greatly relieved in his breathing that he slept whenever he was left undisturbed, and he remained free from dyspnœa all night.

At two hours and at four hours after the administration, the pulse possessed the characters represented in the next two tracings. (Figs. 17 and 18.)

Fig. 17.—Robert B. Two hours after nitrite of sodium. Pulse 68, respirations 18 per minute.

Fig. 18.—Robert B. Four hours after nitrite of sodium. Pulse 64, respirations 18 per minute.

On other occasions similar satisfactory results were obtained on this patient with nitrite of sodium and also with nitro-glycerine. The latter, however, several times produced severe headache, and, therefore, nitrite of sodium was more frequently given. While five-grain doses of it in a most marked manner subdued the severe paroxysms of dyspnœa—the patient on one occasion stating that he would have died had the medicine not relieved him—it did not cause any headache. At the same time it was found that the dyspnœa could, in this patient, generally be relieved by one or two grain doses. One administration, but only one out of a considerable number, of five grains was followed by toxic symptoms, consisting mainly of great feebleness of the circulation, which, however, quickly disappeared after the administration of a little brandy.

The administration by the stomach of nitrite of amyl, nitrite of ethyl, nitrite of sodium, and nitro-glycerine, therefore, produced the same kind of effect on asthma as that which followed the administration by inhalation of the volatile of these nitrites. A marked, and for therapeutic purposes a very important difference, was manifested in the duration of these effects, which were greatly prolonged by stomach administration.

It has been well recognised that the auscultatory phenomena, which have been referred to, are present during the asthmatic paroxysm. It does not appear to have been distinctly appreciated that they are so intimately associated with the paroxysms, that dyspnœa is present only while they are present, and that it subsides or disappears only when they subside or disappear. Not only has this been rendered apparent by the observations I have described, but also by an observation in which the exceptional result was obtained, that a nitrite administered during a severe asthmatic paroxysm failed to produce more than an insignificant and temporary improvement in the dyspnœa, and equally failed to subdue more than to a slight extent, and for a brief period, the loud rhonchi and sibili that were present.

The observations that have been described further show that both the dyspnœa and the sounds in the chest can be made to disappear simultaneously, or nearly so, by substances whose action is to reduce, powerfully, the contractility of non-striped muscle. It appears to follow from this that the dyspnœa of asthma is caused by spasm of the bronchial muscles.

The view that this dyspnœa finds its chief explanation in spasm of the diaphragm, associated or not associated with spasm of the ordinary muscles of respiration, has, as I have already stated, received so damaging a criticism from Biermer, that its further refutation by such observations as have been brought forward seems to be almost unnecessary. The remaining view to which any importance may be attached, that, namely, of constriction of the bronchial tubes by swellings of a hyperæmic, herpetic, or

urticaria-like character—whose most prominent upholders are Weber and Sir Andrew Clark—presupposes for the production of the swellings a dilated state of the bloodvessels of the bronchial tubes. The means which I have successfully employed, however, for controlling and checking the asthmatic paroxysm are the very means which should, according to this theory, be the most efficient that could have been selected for increasing the paroxysm and rendering it more prolonged. There is no fact in pharmacology more certain and undoubted than that nitrites produce rapid and great dilatation of the bloodvessels throughout the body.[1] In the first observation I brought forward, and I have others of a like kind, this dilatation was produced at the moment when the dyspnœa disappeared; it was maintained while the dyspnœa was absent; and it gave place to a normal condition of the bloodvessels when the dyspnœa returned. It seems, therefore, to have been abundantly shown that the theory of the production of asthmatic dyspnœa, by swellings of the bronchial mucous membrane of a hyperæmic or inflammatory kind, can no longer be maintained.

The conceptions of the conditions that immediately produce the asthmatic dyspnœa or orthopnœa have been obscured by the numerous and unharmonizing theories that have been propounded. If the results of the observations I have brought forward should produce the impression upon others which they have produced upon me, I believe these obscurities will to a great extent disappear, and the old doctrine, that the asthmatic paroxysm depends immediately upon spasm of the bronchial muscles, will be more firmly established in the position which it had formerly occupied. At the same time, it is not to be supposed that this doctrine is incompatible with the view that, in a secondary manner, and as a result probably of the dyspnœa which has already been caused by contractions of the bronchial muscles, spasmodic contractions may also be originated in the diaphragm and in other of the ordinary muscles of respiration.

The success in any disease of a therapeutic agent, whose action is a known one, affords valuable evidence of the correctness of the theory of the causation of that disease. Such evidence appears to be afforded in a very incisive manner by the influence of nitrites in asthma. In this disease many other remedies have also been found to produce benefit. Probably this benefit has been more markedly associated with the inhalation of the smoke of certain solanaceous plants, of nitre, and of several patent medicines in the

[1] Although it has not been proved by direct observation that nitrites dilate the bloodvessels on the surface of the bronchi, there is no reason to doubt that they do so; while the fact that these bloodvessels are derived from the aorta and intercostal arteries, and that they possess the same structure as the other bloodvessels of the systemic circulation, afford a strong presumption in favour of their being dilated by nitrites in common with the other bloodvessels of this system.

form of powders, than with any other remedies. The cause of the benefit which these substances produce is, however, almost unknown, and such speculations have been advanced as those of Oertel in his *Treatise on Respiratory Therapeutics*,[1] that the fumes of stramonium and of nitre are beneficial because they stimulate the air passages, giving rise to violent coughing and copious expectoration, and not because they act anæsthetically and antispasmodically on the bronchioles and lungs. Their influence upon the essential phenomena of asthma, and especially upon those phenomena that imply spasm of the bronchial tubes has not, indeed, been investigated, nor is there much knowledge as to the composition of the patent asthma remedies. The extensive use of these remedies suggests that advantage must be gained from their employment; and it is a common experience to meet with patients who have a greater faith in their power to give relief, than in the arsenic, or iodide of potassium, or lobelia which may be recommended to them by their medical advisers. So much have I been impressed with this circumstance, that I have procured several of these patent medicines for the purpose of having their composition, and the composition of the products of their combustion, determined. This has been done for me by my assistant, Dr Atkinson, with the results noted in the subjoined table:—

	Before burning, infusion made with water contains			After burning, smoke contains	
	Nitrite.	Nitrate.	Pupil dilator.	Nitrite.	Pupil dilator.
1. Maokill's Asthma Cure (Hamilton)	None	Distinctly	Distinctly	Distinctly	Distinctly
2. Himrod's Asthma Cure (Himrod Manufacturing Co.)	,,	Abundantly	,,	Abundantly	,,
3. Hinksman (Carluke)	,,	Distinctly	,,	Distinctly	,,
4. Senier's Asthma Remedy (London and Milwaukee)	,,	Trace	,,	None	,,
5. Green Mountain Asthma Cure	,,	,,	,,	,,	,,
6. Binning's Asthma Cure	,,	Distinctly	,,	Distinctly	,,
7. Girdwood's Patent Asthma Cure (Belfast)	,,	,,	,,	,,	,,
8. Edward's "Valley Moss" Asthma Cure	,,	Trace	,,	None	,,
9. Ozone Paper (Huggins, London)	,,	Abundantly	None	Abundantly	None
10. Hockin's Remedy for Asthma and Bronchitis (Ryde, Isle of Wight)	,,	None	Distinctly	None	Distinctly
11. Papier Fruneau contre l'Asthme (Fruneau, Nantes)	,,	Abundantly	None	Abundantly	None
12. Dr Palmer's Antiasthmatic Papers (Simpson & Co., Dublin)	,,	,,	,,	,,	,,
13. Joyes' Cigares Antiasmatiques	,,	Trace	Distinctly	None	Distinctly
14. Argo Cigarettes (Blair, Perth)	,,	Faint Trace	,,	,,	,,
15. Cigarettes Indiennes (Grimault & Cie, Paris)	,,	None	Trace	,,	Faint trace
16. Kay's Stramonium Cigarettes (Stockport)	,,	,,	Distinctly	,,	Distinctly
17. Dr Douglas's Maori Cigarettes (Perth)	,,	Trace	,,	,,	,,
18. Marshall's Cubeb Cigarettes (Horner, New York)	,,	None	Trace	,,	Faint trace

[1] Von Ziemssen's *Handbook of General Therapeutics*. Translated by J. Burney Yeo, M.D., 1885, p. 178.

Arsenic was searched for in all of the above preparations, but was not discovered in any of them. Nitrites were not found in the smoke of any of the cigarettes examined; but of the other preparations, in 66 per cent. the products of combustion contained nitrites, and in large quantity in 50 per cent. of them.

While these results supply a sort of confirmation to the value of nitrites in asthma, which the observations that have been described so strongly suggest, it is undoubtedly the case that the best therapeutic effects are not obtained by the inhalation of nitrites, but by their administration through the stomach. The facts that have been stated seem to justify the assertion that their administration in this manner in asthmatic dyspnœa or orthopnœa is entitled to rank as one of the most valuable of the applications of pharmacology to the treatment of disease, an application at least as valuable as that in the painful angina of aortic disease, to which nitrites are at present almost restricted.

Bronchitis.

Having ascertained that the dyspnœa of asthma and the auscultatory phenomena which accompany it are produced by spasm of the bronchial tubes, I next applied the same method of investigation to the dyspnœa of bronchitis, where also dry râles, having the same characters as those that occur in asthma, are met with. In bronchitis, the dyspnœa is undoubtedly a symptom which is less urgent than in asthma, but still it is often so prominent as to add greatly to the distress of the patient. Its causation is admittedly a more complex one in bronchitis than it is in asthma. In the former disease, it is usually associated with physical signs of a more varied description; for it may be accompanied not only with dry râles, but also with many varieties of moist sounds. The explanation of the production of the latter is not, so far as I know, a matter of doubt or ambiguity, but some difference of opinion exists as to the explanation of the former.

The impression in my own mind has until lately been that the dry râles, the rhonchi and sibili, the snoring, cooing, and whistling sounds, are produced by swelling or engorgement of the mucous lining of the bronchial tubes, or by constrictions of these tubes caused by deposits of adhesive mucus or other products of inflammation; and that these sounds, because they were indications of these or similar changes in the bronchial tubes, were among the most important of the symptoms of bronchial inflammation.

A spasm element, whose influence upon the physical phenomena of bronchitis was, however, by no means easily definable, entered into the conception of the disease in those cases where dyspnœa was specially urgent, or where it interrupted the

ordinary course of an otherwise continuous slight dyspnœa by periodically assuming exacerbations in the intensity of its manifestations.

A reference to the literature of bronchitis has, on the whole, confirmed the impression that what I have stated is the prevailing opinion, and the prevailing teaching on the subject. For example, the dry sounds of bronchitis, the rhonchi and sibili, are stated by Laennec,[1] Guttmann,[2] Davis,[3] Latham,[4] Hilton, Fagge,[5] Riegel,[6] Jaccoud,[7] and others, to be produced by contractions of the bronchial tubes, caused by tenacious mucus, tumefaction, engorgement, or puckerings of the mucous lining. Only a few writers, such as Niemeyer,[8] Stokes,[9] Roberts,[10] and Carmichael,[11] state that it is occasionally indicated by these sounds that the bronchi are being constricted by spasm of their muscles.

The conceptions generally prevalent on the subject may perhaps be best illustrated by the following quotations:—

Riegel, in his elaborate dissertation on bronchial catarrh, contributed to Ziemssen's *Cyclopædia of the Practice of Medicine*, states:

"The accurate determination of the character of the râles [in bronchial catarrh] is of especial importance, because we can determine thereby the special sort of alteration existing in the bronchial tubes. Thus the long-used distinction between moist and dry râles has an important significance. The former are due to the movement of thin liquid products in the trachea and bronchi, and the latter are due to the friction of the current of air against the swollen mucous membrane of the bronchi, and to the presence of very viscid products. Dry râles indicate, therefore, more or less considerable swelling of the mucous membrane, and eventually the presence of small quantities of very tenacious fluid in the bronchi."[12]

In another place, having referred to the effects of secretion in the air tubes, he proceeds to state:

"In other cases, only dry, whistling, and sonorous râles are heard, occasioned by severe swelling of the mucous membrane, and the presence of tenacious, scanty secretion."[13]

[1] *A Treatise on Mediate Auscultation.* Edited by Theophilus Herbert, M.D., pp. 52, 53, 61, 64, 73, 74, 78. London, 1846.

[2] *Handbook of Physical Diagnosis.* Translated for the New Sydenham Society by Alexander Napier, M.D. 1879, pp. 159, 160.

[3] Pepper's *System of Medicine*, 1885, vol. iii. pp. 171, 178.

[4] *Collected Works.* Edited for the New Sydenham Society by Dr R. Martin. 1878, vol. ii. pp. 112, 113, 116, 117, 120.

[5] *The Principles and Practice of Medicine*, 1886, vol. i. pp. 863, 864.

[6] Ziemssen's *Cyclopædia of the Practice of Medicine*, 1877, vol. iv. pp. 354, 388, 427.

[7] *Traité de pathologie interne*, 1883, t. ii. pp. 378, 381, 382.

[8] *A Text-book of Practical Medicine.* Translated by Geo. H. Humphreys, M.D. 1870, vol. i. p. 82.

[9] *A Treatise on the Diagnosis and Treatment of Diseases of the Chest.* Edited for the New Sydenham Society by Alfred Hudson, M.D. 1882, p. 64.

[10] Reynold's *System of Medicine*, 1871, vol. iii. pp. 891, 896.

[11] *Edinburgh Medical Journal*, Oct. and Nov. 1886.

[12] *Loc. cit.*, p. 354.

[13] *Loc. cit.*, p. 388.

Bristowe, in his *Treatise on the Theory and Practice of Medicine*, thus explains these sounds :[1]

"The cause of rhonchus is not the bursting of bubbles or the passage of air through fluid, but the passage of air through a tube narrowed at some point either by thickening of its parietes or by the adhesion of a plug of tenacious mucus." . . . . "The pitch of the musical note depends on various complex conditions, the exact influence of each one of which it would be difficult to estimate, but is determined in very considerable degree by the size of the bronchial tube in which it is developed. Thus, as a general rule, hissing and whistling sounds, or sibilant rhonchi, arise in the smaller tubes, and grave tones or sonorous rhonchi are the product of the larger ones."

Many quotations to the same effect could be extracted from the writings of other authors.

Putting aside as a cause of dyspnœa the moist sounds, which in bronchitis imply, according to their abundance, either obstruction to the movement of air in the bronchi, or obstruction to the contact of air with the bloodvessels in the air cells, there remain for consideration the dry sounds of the different qualities of rhonchi and sibili, which share with the moist sounds a peculiar diagnostic importance in bronchitis.

A number of observations were made with the object of determining to what extent these sounds are modified by nitrites, and to what extent any modification produced was associated with a change in the severity of the dyspnœa that was present.

The observations were made in many forms and stages of bronchitis, but for the purpose I have in view they may be arranged in accordance with the characters of the expectoration, as, for instance, if that were mucopurulent, or serous, or glairy and adhesive, or abundant or scanty. The effects of nitrites on the dyspnœa and auscultatory phenomena, where such like variations in the expectoration existed, may be illustrated by a brief description of a few observations selected from many others that were made. In this selection, observations have been taken which will also serve to illustrate the effects of each of the nitrites administered, and of nitro-glycerine.

Observation IX.—Daniel M'D., a carter, aged 44, was admitted into the Royal Infirmary, complaining of cough, profuse expectoration, constant difficulty in breathing and general weakness. He had been troubled with cough for twenty years, but had otherwise been healthy. For the last two years he had not been able to work. His chest was somewhat barrel-shaped, and there was a hyper-resonant note over the whole of the anterior surface. The auscultatory phenomena were those of bronchitis, viz., prolonged expiration, numerous median crepitations, and an abundance of rhonchi and sibili. The heart was dilated slightly, but there was no evidence of disease of the valves.

On the 6th of October 1886, immediately before nitro-glycerine

[1] Third edition, 1884, pp. 386, 387.

was administered, the following conditions were present: The breathing was "a little difficult," the chest feeling "very stiff." Since early morning he had expectorated a large quantity of muco-purulent sputum. At the right side there was snoring rhonchus with crepitations during inspiration, and brief rhonchus during expiration; and at the left side there was sibilus during inspiration and expiration, expiration being considerably prolonged at both sides. The pulse was 100, and the respirations were 25 per minute. At 11 35′ A.M. there were rhonchi throughout inspiration and expiration at both sides, with a few crepitations which occurred occasionally.

FIG. 19.—Before nitro-glycerine; pulse 100, respirations 26.

At 11 36′, four minims of a 1 per cent. solution of nitro-glycerine were administered in a little water.

At 11 36′ 30″, at both sides the rhonchi and sibili had entirely disappeared, a few crepitations only remaining; and the patient said he "felt much relieved."

At 11 40′, the pulse was 98, and the respirations were 30 per minute.

FIG. 20.—Four minutes after nitro-glycerine; pulse 98, respirations 30.

At 11 41′, at the right side the breathing was quite soft, and at the left side it had the same character, but a faint distant rhonchus was now and then heard.

At 11 45′, the pulse was 102, and the respirations were 30 per minute.

FIG. 21.—Nine minutes after nitro-glycerine; pulse 102, respirations 30.

At 11 48′, the breathing was perfectly soft, and free from all accompaniments at both sides. The patient stated that he has no feeling of tightness, and that his breathing is "quite easy."

From 11 51′ to 12 38′ the chest was almost continuously auscultated, and during the whole of this time the breathing continued to be soft and vesicular, and free from rhonchi and sibili; the only accompaniments being small and medium crepitations, which were usually, but not invariably, present. During the whole of this time, also, the breathing of the patient remained altogether easy

and unembarrassed. The pulse and respirations were usually slightly less frequent than they had been before the administration of the nitro-glycerine.

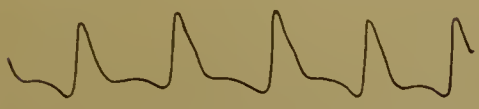

FIG. 22.—Eighteen minutes after nitro-glycerine; pulse 99, respirations 27.

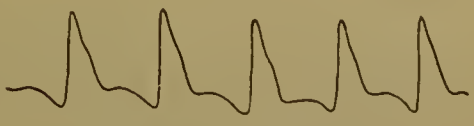

FIG. 23.—Thirty-four minutes after nitro-glycerine; pulse 101, respirations 27.

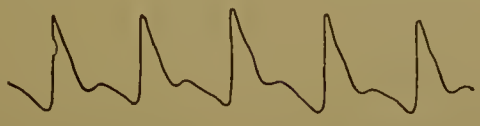

FIG. 24.—One hour and two minutes after nitro-glycerine; pulse 96, respirations 27.

The uniformity of the conditions during frequent observations led to the observations being interrupted for a short time, when they were resumed.

At 1 2′ P.M., at the right side there were sibili with inspiration and expiration, and at the left side there were faint sibili, varied by occasional rhonchi, accompanying both inspiration and expiration. Crepitations were also heard at both sides during inspiration and expiration. The patient said his "chest was a little stiffer." The pulse was 96, and the respirations were 25 per minute.

FIG. 25.—One hour and twenty-nine minutes after nitro-glycerine; pulse 96, respirations 25.

At 1 6′, however, while the crepitations continued, the rhonchi and sibili had again entirely disappeared; and the patient said his "breath was light again."

At 1 26′, at the right side there were slight sibilant rhonchi, and at the left side there were sibili and a few crepitations, with both inspiration and expiration. The breathing had become more difficult, according to the patient. The pulse was 84, and the respirations were 31 per minute.

FIG. 26.—One hour and fifty-one minutes after nitro-glycerine; pulse 84, respirations 31.

At 1 42′, the patient was again easier in his breathing, and the rhonchi and sibili had again disappeared.

Fig. 27.—Two hours and thirteen minutes after nitro-glycerine; pulse 84, respirations 26.

At 2, the only accompaniments at the right side were crepitations, but a slight sibilus occurred with crepitations at the left side. The patient stated that his breathing was "fairly easy."

Fig. 23.—Two hours and twenty-four minutes after nitro-glycerine; pulse 82, respirations 24.

The breathing continued to be fairly easy until 5 P.M., when the sensations of tightness and difficulty reappeared; and it was found that rhonchi, sibili, and crepitations were continuous during the respirations.

Observation X.—The second observation in bronchitis, which I wish to describe, was made with nitrite of ethyl.

The patient, Annie M., 53 years of age, a washerwoman, was admitted into the Royal Infirmary on the 30th of December 1885, complaining of pain in the chest and side, difficulty of breathing, and constant cough with much expectoration. Two years previously she had suffered from some acute chest affection following exposure to wet. During the winter of 1884–85 she had suffered from a severe cold with cough, and the cough did not entirely disappear until summer. Four weeks before her admission she again had a cold, and her old troubles all returned. Treatment at home having produced little benefit, she applied for admission into the Royal Infirmary. When examined, she was found to be a well-built, strong woman, with an anxious, suffering expression. Her cough was frequent and violent, and was found to be associated with extensive bronchitis. There was a little emphysema, but no cardiac lesion could be detected. The expectoration was considerable in quantity, mucopurulent, and frothy.

On the 31st of December, the day following her admission, the symptoms had not materially changed.

At 1 15′ to 1 18′ P.M., over the front of the chest on both sides there were numerous sibili and rhonchi with inspiration and expiration. The pulse was 90, and the respirations were 20 per minute.

At 1 20′, she received two minims of a fifty per cent. alcoholic solution of nitrite of ethyl, diffused through two drachms of water.

At 1 22′, the only accompaniment heard with the breathing was an occasional brief rhonchus with expiration. She said her "breath feels easier."

At 1 23′, the breath sounds were entirely free from any accompaniment. The pulse was 90, and the respirations were 18 per minute.

At 1 24′, 1 26′, and 1 27′, this freedom from accompaniments continued without any interruption whatever.

At 1 30′, however, there were occasionally faint rhonchi at the end of inspiration, which, at 1 32′, were converted into sibili. The pulse was now 88, and the respirations sixteen per minute.

At 1 34′, the rhonchi and sibili had again disappeared, and they remained absent, and the breathing continued unembarrassed until 2 P.M., when the observations were interrupted. The patient was not again examined until 8 P.M., when she said the breathing had a short time previously become as difficult, and the chest tightness as great as it had been before she had received the dose of nitrite of ethyl. Rhonchi and sibili were found to be continuous over the front of the chest, and the respiratory movements were found to be laboured.

Observation XI.—The third observation I shall describe was on a patient, Annie M., 19 years of age, who had suffered for some years from several diseases of the lungs, including pleurisy and bronchitis. She came under my care on the 9th of September 1886, complaining of pain in the chest, difficulty of breathing, and cough. Besides the symptoms of widely extended bronchitis, there was also evidence of old pleurisy, and of a lingering pneumonic inflammation at the back of the chest, both of which proved extremely refractory to treatment.

On the 11th of December 1886, at 12 50′ P.M., it was found that, at the front of the chest, there were at the right side sibili during inspiration, and rhonchi during the whole of expiration; and at the left side, sibili during inspiration, and harsh breathing with creaking sounds during expiration. The sputum was considerable in quantity, and consisted of rather viscid, frothy serum, having mixed with it a few masses of purulent matter. The pulse was 100, and the respirations 30 per minute.

Fig. 29.—Two minutes before nitrite of amyl; pulse 100, respirations 30.

At 12 57′, the patient received four minims of nitrite of amyl, diffused through a little water.

At 12 57′ 30′, the face had become red.

Fig. 30.—One minute after nitrite of amyl; pulse 115, respirations 32.

At 12 58′ to 59′, at the right side there were only crepitations with inspiration, and a little creaking with a few crepitations with expiration; while at the left side inspiration was harsh, but without accompaniment, and expiration had only a little creaking at its termination.

At 1 P.M., the blush had almost disappeared from the face.

At 1 1′, the pulse was 99, and the respirations were 25 per minute. Rhonchi and sibili were still entirely absent.

At 1 2′, a sibilus occasionally was heard during inspiration at the left side.

At 1 4′, a similar accompaniment was now again heard at the right side.

Fig. 31.—Eight minutes after nitrite of amyl; pulse 99, respirations 32.

At 1 5′, however, neither sibili nor rhonchi were heard anywhere at the front of the chest, and they continued to be entirely absent until 1 17′, although inspiration frequently became harsh, and crepitations and creaking sounds were generally to be heard.

At 1 19′, now and then a short sibilus accompanied inspiration at the left side.

At 1 20′, sibili were frequently heard during expiration at the right side.

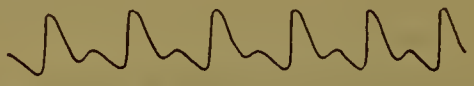

Fig. 32.—Twenty-eight minutes after nitrite of amyl; pulse 106, respirations 30.

Rhonchi by-and-by added themselves to the sibili, until at 1 30′, or thirty-three minutes after the administration, the auscultatory phenomena had returned to very much the same condition as they had been before the patient had received nitrite of amyl. The pulse tracings show that the effects on the circulation were of much longer duration than on the dyspnœa and its associated auscultatory phenomena.

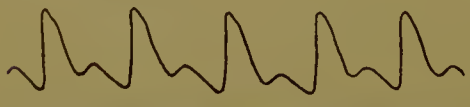

Fig. 33.—Forty-one minutes after nitrite of amyl; pulse 100, respirations 32.

Fig. 34.—One hour and forty-three minutes after nitrite of amyl; pulse 92, respirations 32.

Observation XII.—In the next observation, the fourth in bronchitis, the effects of nitrites in bronchitis accompanied with an adhesive and scanty sputum are illustrated.

The patient, Alexander G., 49 years of age, had suffered, at intervals, for fifteen years before his admission into the Royal

Infirmary, from bronchitis. Each attack was referred by him to a special "wetting" which he got while following his occupation as a shepherd. He had also had a long experience of rheumatic pains. He was a tall, well-built man; and his chief complaints were breathlessness, cough, frequently occurring in paroxysms of great severity, and great difficulty in expectoration. The lungs were found to be emphysematous, and to be affected with extensive bronchitis associated with a scanty, glairy sputum of small quantity. Nitrites were on many occasions administered to this patient, but the details of only two of these administrations will be here given: the first with nitrite of sodium, and the second with nitrite of ethyl.

On the 28th of November 1885, on examining the chest at 1 6′ P.M., sibili, now and then varied with rhonchi, were heard almost continuously with inspiration and expiration. The pulse was 56, and the respirations were 16 per minute.

At 1 9′ 15″, one grain of nitrite of sodium, dissolved in about a drachm of water, was given to the patient.

At 1 10′ 10″, the sibili and rhonchi had entirely disappeared, and the breathing was no longer difficult. From this time until 1 52′, a period of forty-two minutes, frequent examinations of the chest showed that the breath-sounds remained absolutely free from rhonchi or sibili.

At 1 52′ 30″, however, faint sibili were heard at the end of expiration, and the patient said his breathing was "beginning to close up again."

At 1 55′, sibilus was frequent with expiration at the right side.

At 1 63′, rhonchus was present at both sides, and the breathing was as difficult as it had been originally.

Observation XIII.—An observation on this patient with nitrite of ethyl was made on the 24th of November 1885.

At 10 40′ A.M., it was found that over both lungs inspiration and expiration were accompanied with nearly continuous sibili, the pulse being 63 per minute.

Fig. 35.—Immediately before nitrite of ethyl; pulse 66.

At 10 42′, two drachms of spiritus ætheris nitrosi (Phar. Brit.), estimated by an analysis to contain nearly two minims of nitrite of ethyl, were given to the patient.

At 10 43′, he said his breathing was easier.

Fig. 36.—Two minutes thirty sec. after nitrite of ethyl; pulse 70.

At 10 45′, the sibili had entirely disappeared. The respiratory sounds remained absolutely free from accompaniments until 12 noon, or for a period of an hour and a quarter.

FIG. 37.—Five minutes after nitrite of ethyl; pulse 74.

FIG. 38.—Thirteen minutes after nitrite of ethyl; pulse 72.

FIG. 39.—Twenty-three minutes after nitrite of ethyl; pulse 72.

FIG. 40.—Fifty-eight minutes after nitrite of ethyl; pulse 66.

The chest was not again examined until 12 30′, and then rhonchi were heard with inspiration and sibili with expiration.

FIG. 41.—One hour and forty-eight minutes after nitrite of ethyl; pulse 63.

These accompaniments were found to persist in subsequent examinations, while the breathing gradually became more difficult.

FIG. 42.—Two hours and eighteen minutes after nitrite of ethyl; pulse 60.

OBSERVATION XIV.—One of the best illustrations of the influence of nitrites on the dyspnœa and associated auscultatory phenomena of bronchitis was obtained in an observation on Thomas H., to whose case I have already referred when describing an observation made during a paroxysm of asthma which was treated with nitro-glycerine. I then alluded to the circumstance that several observations had been made on him when he was not suffering from asthmatic paroxysms, for the purpose of ascertaining the effects of nitrites on the symptoms of bronchitis, from which he also suffered during a portion of the time that he was under treatment in the hospital.

When the observation I wish now to describe was made, he had comparatively slight dyspnœa—the chief evidence of which was merely a sensation of weight and tightness in the chest.

At 1 20′ P.M., on the 12th of February 1887, it was found that at the right side inspiration was harsh, and accompanied with several coarse crepitations, and with occasional rhonchus; while the latter half of expiration consisted of a loud rhonchus. At the left side the conditions were the same, except that there were no crepitations, and that sibili and rhonchi occupied the whole period of expiration. There was no expectoration, nor had there been any

during the previous two hours. The pulse was 75, and the respirations were 20 per minute.

At 1 30′ 30″, he received ten minims of a 10 per cent. solution of nitrite of sodium (1 gr.) diluted with a drachm of water.

At 1 33′, at the left side there were a few crepitations with inspiration, but no accompaniments with expiration; and at the right side the breath sounds were absolutely clear. The patient stated that the sensations of weight and tightness had disappeared from his chest, and that his breathing was "quite easy."

At 1 34′, the conditions of the breathing and of the breath sounds remained the same as at 1 33′.

At 1 35′, however, slight rhonchus was heard during a part of inspiration and of expiration over both lungs, and the patient said the breathing was "not quite so clear."

At 1 36′ 30″, he said the breathing was again "clear," and it was found that there were no longer any rhonchi at the left side, and only on occasions a slight rhonchus with inspiration at the right side.

At 1 37′, and at 1 38′ 30″, both sides were entirely free from any other accompaniment than a few crepitations, and the breathing was entirely unembarrassed.

At 1 42′ to 1 46′, brief rhonchi were occasionally heard with expiration, sometimes at the right, and at other times at the left side.

At 1 47′ to 1 55′, the breath sounds were again entirely free from rhonchi and sibili, and there was no dyspnœa.

At 1 57′, rhonchi were occasionally heard with inspiration and expiration at the right side.

At 1 59′, they had again disappeared, and they continued to be absent until 2 5′, when again a rhonchus or sibilus was heard at one or other side, and with either inspiration or expiration. No further change occurred until 2 13′, when these accompaniments were found to have disappeared, and they had not again returned at 2 40′, when the observations were stopped. While the accompaniments were absent there was absolutely no feeling of weight or tightness in the chest.

The effects on the pulse tension were rather slowly developed, but, as the three subjoined tracings show, they had not disappeared at the conclusion of the observation. There had been neither cough nor expectoration during the whole time following the administration of the nitrite.

Fig. 43.—Before nitrite of sodium; pulse 76, respirations 20.

Fig. 44.—Twenty minutes after nitrite of sodium; pulse 78, respirations 19.

Fig. 45.—One hour and ten minutes after nitrite of sodium; pulse 73, respirations 18.

The last observation I propose to describe affords an illustration of the effects of a nitrite in bronchitis accompanied with profuse watery expectoration.

Observation XV.—The patient, Mary B., 30 years of age, became ill with bronchitis four months before her admission into the Royal Infirmary, in December 1886. She suffered, on admission, from palpitation, dyspnœa, and a frequent cough, with much watery and frothy expectoration. There was no disease of the heart, nor marked emphysema.

On the 16th of December, at 1 52′, rhonchi were heard profusely over all parts of the front of the chest, along with numerous small and medium crepitations.

At 1 54′, she received two minims of nitrite of amyl in one drachm of water.

At 1 57′, there were no rhonchi or sibili heard anywhere, and the patient stated that her breathing was much easier.

At 2 2′, the auscultatory phenomena and the breathing were the same as at 1 57′.

At 2 5′, however, rhonchi were heard at the right side, though only rarely. They, however, gradually became more frequent, and the breathing slowly reacquired its former dyspnœic character.

Including those that have now been described, sixty-one observations were made in bronchitis, of which detailed records have been preserved. In forty-eight of them the nitrite administered succeeded in removing every vestige of rhonchus or sibilus for various periods of time. In ten these sounds were lessened in their amount, but they were not altogether silenced. In only three the effects were either extremely slight, or altogether negative. The sixty-one observations were made on twenty-five patients suffering from bronchitis.

Whenever rhonchi or sibili associated with any sensation of dyspnœa were removed, the previously existing dyspnœa disappeared, or became much less marked during at least the time when the rhonchi and sibili were absent or lessened; but when nitrites failed to silence or to reduce the rhonchi or sibili they also invariably failed appreciably to lessen the dyspnœa.

It seems to me that the demonstration is complete that the dyspnœa of bronchitis, when associated with rhonchi and sibili, is mainly produced by the conditions of the bronchial tubes which produce the rhonchi and sibili. The cause of these sounds cannot be intumescence by congestion of bloodvessels or other results of inflammation, otherwise nitrites would increase, rather than lessen or suspend, the sounds. Adhesive mucus cannot frequently be a cause, otherwise nitrites would not, in so large a proportion of the observations, have succeeded in producing complete silence; for they have no special effect on deposited mucus, nor was it found

that any particular influence was exerted by them upon the frequency of expectoration. The only explanation of the results of the observations that can reasonably be adopted, seems to be that in bronchitis the rhonchi and sibili are frequently produced by contractions of the bronchial muscles; that dyspnœa is produced by the impeded movement of air caused by the constrictions resulting from these contractions; and that both are removed by nitrites, because nitrites reduce the spasmodic contractions of the bronchial muscles.

I have been much gratified to find that the conclusions thus arrived at are in complete harmony with opinions expressed many years ago by my former teacher, Professor Gairdner. Writing, in 1853, on the subject of bronchitis, he states:[1] "As our information at present stands, we must confess ourselves to be unhesitating believers in the doctrine of spasm. We even go further, and think there is good ground for supposing partial spasm to be in all cases connected with bronchitis, especially in its early stages, and to be the chief cause of that narrowing of the tubes at particular points, which is the most probable mechanical condition producing the sonorous and sibilant râles."

In a considerable number of instances nitrites succeeded in completely controlling the spasmodic contractions of the bronchial muscles for only brief periods of time, presenting a marked contrast in the duration of their beneficial effects in bronchitis to what was usually observed when they were administered in an asthmatic paroxysm. The explanation of this may probably be found in the circumstance that in bronchitis, as contrasted with asthma, the exciting cause of the spasm is a persisting and purely local one, which is not removed by the action of nitrites, but continues so long as the bronchial inflammation continues.

Still, in all but the relatively few instances where the effects were practically negative, it was found that relief was experienced for a long time after the rhonchi and sibili had returned; indeed, in many of the observations for several hours. The administration of a nitrite does not, therefore, require to be a very frequently repeated one; as the dry sounds, which sometimes quickly reappear, are still for a long time present only in a degree and amount which is much less than they originally possessed. It is, in most cases, unnecessary to administer the nitrite that is selected more frequently than every three or four hours.

Although nitrites dilate bloodvessels at the same time as they relieve the dyspnœa produced by spasm of the bronchial muscle, it has never occurred in these observations that they have increased the bronchial inflammation. Their action, when they subdued or lessened the dry râles, was invariably to give relief to the patient; in some cases this relief was apparent even on the day following that in which a single dose had been administered; and, in a few

[1] *British and Foreign Medico-Chirurgical Review*, 1853, vol. xi. p. 477.

instances, bronchitis was altogether cured by their almost unaided influence. At the same time, I should anticipate that where marked tendency to bronchial or pulmonary hæmorrhage exists, they may increase this tendency, and, therefore, prove injurious.

I have not obtained any facts that would justify the assertion that any one of the nitrites is to be preferred in bronchitis, because it possesses therapeutic advantages over the others. There are, however, advantages of other kinds which lead me to give a preference to nitrite of sodium, and to nitro-glycerine. Each of these is stable, and can be used in solution, which admits of ready administration by the stomach, or by subcutaneous injection, in doses that can be accurately defined. Nitro-glycerine[1] may, therefore, be conveniently given, not only in the form of tablets of the British *Pharmacopœia*, but also dissolved in absolute alcohol, or rectified spirit, or distilled water; bearing in mind that a saturated solution of 1 in 760 or 800 of distilled water can be obtained only by prolonged contact, that a solution in ordinary water slowly undergoes decomposition, and that solutions cannot be kept unchanged for many days in the presence of alkalies or alkaline salts. On the other hand, nitrite of sodium is freely soluble in water, and it remains unchanged for an indefinite time when dissolved in either distilled or ordinary water; but it is decomposed by acids, and for this reason it is quite possible that when the contents of the stomach are exceptionally acid in reaction the nitrous anhydride it contains may be so completely set free in the stomach that only a little nitrite will enter the blood—an accident, however, which could easily be prevented by giving it with an alkali.

Nitrite of amyl and nitrite of ethyl have not only the inconvenience of requiring alcohol to dissolve them, but also the great disadvantage of being very unstable substances, spontaneously undergoing change and deteriorating in the course of time. These inconveniences are fully recognised in the case of nitrate of ethyl, as it occurs in the *spiritus ætheris nitrosi* of the *Pharmacopœia*, which, however, has continued, notwithstanding, to be a favourite and widely used remedy. It is probable that the favour with which it is regarded is due not only to the action on the circulation which it shares with the other nitrites, and to its being an alcoholic preparation, but also to the previously unrecognised influence which it exerts on dyspnœa, when it is administered, as it so frequently is, in the treatment of bronchial catarrh.

The power of these substances to control bronchial spasm, whether that show itself in the orthopnœa of an asthmatic paroxysm or in the relatively slight dyspnœa of ordinary bronchitis, will probably lead to their being more largely used than they have hitherto been in the treatment of disease. Where their administration is

[1] The prejudices that are sometimes raised by the use of this word may be avoided by prescribing it under the name of "Trinitrine."

successful in removing the auscultatory evidences of such spasm, it is difficult to imagine anything more convincing of the influence that may be exerted upon the conditions of disease by pharmacological agencies. The observer has presented to him a patient in whose thorax a continuous succession of varying sounds is being produced, and whose condition is one of distress, and sometimes of intense suffering and anxiety; within a few moments after a nitrite has been administered the conditions are entirely changed; the endless succession of noisy breath-accompaniments gives place to an almost complete silence, in which only the subdued quiet of the normal respiratory sounds is audible; and, at the same time, the distress of dyspnœa, or, it may be, the intense suffering and anxiety of urgent orthopnœa are entirely removed.

I have, in conclusion, to express my obligations to a number of gentlemen who gave me valuable assistance in these observations, and especially to Dr Sawers Scott, for some time clinical assistant, and to Drs Vaughan, Thompson, Robertson, Wilson, and Jeffcoat, resident physicians, and Messrs Tofft, Traquair, Gibson, Dunlop, Loubser, Hawkes, Hutton, and others of the clinical clerks in my wards when the observations were being made.

As in each observation the chest was almost continuously auscultated, pulse tracings were taken every few minutes, the respiratory and pulse movements were frequently counted, and, in several instances, the movements of the chest and abdomen were recorded by means of Marey's polygraph, while the observations generally lasted for one or two hours, it is obvious that any value they may possess has been largely derived from the assistance and co-operation of these gentlemen.

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